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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,823	06/20/2006	Ping Wang	133088.00901(P35703US)	6146

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
11/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,823	WANG ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11 and 13-31* is/are pending in the application.

4a) Of the above claim(s) *8,9,11 and 13-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. **Claims 1 – 9, 11, and 13 – 31 are pending.**

2. Applicant's election of Group I (claims 1 – 9 and 28 – 31, drawn to a composition comprising isolated inverted microsomes in association with a peptide antigen and an MHC protein, and a kit comprising said composition) in the reply filed on 09/13/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant further elected the species of "IL-2" as the costimulatory molecule and "viral, bacterial, yeast, fungal, or protozoan" as the source of the antigen.

It is noted that examination has been extended to include the species of "auto-antigen."

Claims 8 – 9, 11, and 13 – 27 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions or species, there being no allowable generic or linking claim.

Claims 1 – 7 and 28 – 31 are under consideration in the instant application.

3. Receipt is acknowledged of foreign priority papers submitted under 35 U.S.C. 119(a)-(d), which papers are of record in the file of the instant application.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, e.g. on page 5. Applicant is required to delete this and any other instances of embedded hyperlinks and/or other forms of browser-executable code. Embedded hyperlinks and/or other forms of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. See MPEP § 608.01.

5. Claims 29 and 31 are objected to because of the following informality: the claims must end in a period. Appropriate correction is required.

6. The following is a quotation of the **second paragraph of 35 U.S.C. 112**.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1 – 7 and 28 – 31 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 – 7 and 28 – 31 are indefinite in the recitation of "an externally disposed peptide antigen and a protein of the Major Histocompatibility Complex (MHC)" in claim 1, because it is unclear whether or not the limitation "externally disposed" applies the "protein of the MHC." Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

8. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 – 7 and 28 – 31 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The specification does not enable one of skill in the art to make and use the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

A skilled artisan at the time the invention was made was aware that a "vaccine" is a composition which has a prophylactic or therapeutic effect, i.e. the composition must possess the properties of a prophylactically or therapeutically effective adjuvant.

The instant specification discloses at pages 39 – 40 that microsomes of the inventions induce an OVA-specific immune response in vivo. However, given the scope of the claims, limited working examples, the unpredictability in the art and the amount of experimentation required, the amount of direction or guidance provided in the instant specification is not seen as sufficient to enable one of skill in the art to make and use

the claimed invention, i.e. to produce a "vaccine" which has a prophylactic or therapeutic effect, because it is unpredictable whether the claimed composition is usable as a prophylactically or therapeutically effective adjuvant. Fore example, Singh et al. (Nature Biotechnology, 1999, 17: 1075 – 1081; see entire document) review that many experimental adjuvants that appear effective in vitro or even those that progress to clinical trials, have proven too toxic for clinical use (see entire document, in particular, e.g. the abstract, and page 1075, second column, first paragraph).

Therefore, in view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to make and use the claimed invention.

10. Claims 1 and 4 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the claimed composition, because Applicant is not in possession of the recited genus of "costimulatory molecules."

One of skill in the art at the time the invention was made was aware of the existence of numerous structurally and functionally diverse costimulatory molecules, as reviewed e.g. by Greenwald et al. (Annu. Rev. Immunol., 2005, 23: 515 – 548; see entire document). Therefore, the skilled artisan cannot envision all the contemplated costimulatory molecules encompassed by the instant claims.

The written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

11. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 2, and 7 are rejected under **35 U.S.C. 102(b)** as being anticipated by De Lemos-Chiarandini et al. (J. Cell Biol., 1987, 104: 209 – 219; see entire document), alone or as evidenced by the instant specification at page 7, last paragraph.

De Lemos-Chiarandini et al. teach preparations (i.e. compositions) of rat liver microsomes (se entire document, in particular, e.g. page 212, second column), which comprise ruptured vesicles (i.e. membrane fragments) and inverted microsomes (ibid., and Figure 4 – see images labeled by asterisks). Furthermore, De Lemos-Chiarandini et al. teach microsomes which are stored at –70°C (e.g. page 210, "Cell Fractionation Procedures"), while the instant specification at page 7, last paragraph, provides evidence that freeze-thaw treatment of isolated microsomes results in formation of inverted microsomes. Therefore, the reference teaches a composition comprising isolated inverted microsomes from an animal cell.

One of skill in the art is well aware that microsomal membranes comprise membrane proteins (i.e. peptides) exposed on either side of the membrane, and that any protein may be an antigen. Therefore, the composition taught by the reference inherently comprises peptide antigens (i.e. auto-antigens, or normal self-proteins), disposed both internally and externally. Furthermore, with regard to "membrane fragments," the limitation of external v. internal location of the peptide antigen is moot, since both surfaces of the fragment are exposed to the solvent.

Furthermore, one of skill in the art is aware that Class I MHC molecules are expresses on all nucleated cells, including liver cells, and that these molecules are present in endoplasmic reticulum, and hence in any microsome preparation obtained from such cells. Therefore, the composition taught by the reference inherently comprises Class I MHC molecules.

To summarize, when viewed for all it teaches, the reference of De Lemos-Chiarandini et al. teaches a composition comprising isolated inverted microsomes from

an animal cell, which inherently comprise an externally disposed peptide auto-antigen and a protein of the MHC complex. Therefore, the reference teachings anticipate the instant claimed invention.

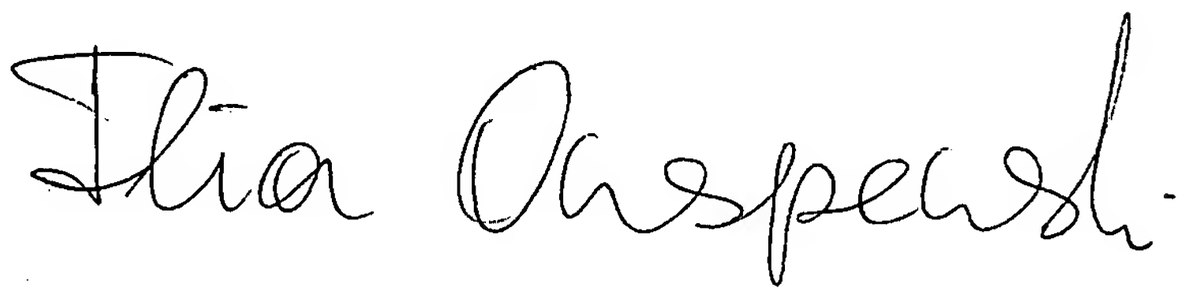
13. Conclusion: no claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ILIA OUSPENSKI, Ph.D.
Patent Examiner
Art Unit 1644



November 16, 2007